UNITED STATES DISTRICT COURT
DISTRICT OF NEVADA

Pacira Pharmaceuticals, Inc.,

Plaintiff

v.

Research Development Foundation,

Defendant

Case No. 2:21-cv-02241-CDS-NJK

Findings of Fact and Conclusions of Law

Pursuant to Federal Rule of Civil Procedure 52(a), I enter my findings of fact and conclusions of law following the bench trial in this case.

I. Findings of Fact

A. About the parties.

1. Plaintiff Pacira Pharmaceuticals, Inc. ("Pacira") is a specialty pharmaceutical company that specializes in products used to treat pain without the use of opioids.

2. Pacira manufactures and sells three FDA-approved products. Relevant here is its EXPAREL® product.

3. EXPAREL® is manufactured via two processes known as the 45L[1] and the 200L respectively. At issue here is the 200L process.

4. Pacira was previously known DepoTech Corporation ("DepoTech"). DepoTech was founded in 1989 by Dr. Kim and Dr. Howell, among others. Both Dr. Kim and Dr. Howell were already working at DepoTech before the '94 Agreement was signed.

[1] Pacira initiated this declaratory action seeking an order from this court that it no longer owes royalties to RDF for either the 45L or 200L processes. I granted Pacira relief from paying royalties for the 45L process at summary judgment. Mot. for summ. j. order, ECF No. 152 at 8–13. I denied summary judgment on the 200L process, so that is the issue that went to trial. CITE. *Id.* at 13–19.

5. In 1999, a company known as SkyePharma, Inc. ("SkyePharma") purchased DepoTech. Then, in 2007, Pacira Biosciences, Pacira Pharmaceuticals' predecessor, purchased SkyePharma.

6. Defendant Research Development Foundation ("RDF") is a Nevada-based non-profit entity. RDF was formed out of a reorganization of the Clayton Foundation for Research in 1989.

7. RDF's mission is to advance medical and scientific research through the transfer of technology from laboratory use to public use "by obtaining patents, granting licenses and administering patents arising out of discoveries pursuant to research conducted or sponsored by certain other charitable organizations."

8. RDF was involved in the formation of DepoTech Corporation, which was incorporated in California in October 1989. RDF was one of the company's initial shareholders.

9. By 1997, DepoTech was involved in the development and manufacture of sustained-release therapeutic products based on a technology known as "DepoFoam."

B. In 1994, Pacira's predecessor DepoTech enters into an agreement with RDF.

10. On February 9, 1994, DepoTech and RDF executed an agreement regarding one patent and three patent applications. "The '94 Agreement".

11. The '94 Agreement was entered into between DepoTech and RDF—it was not entered into between DepoTech and all of RDF's related entities. Pursuant to that agreement, RDF assigned to DepoTech "all right, title, and interest in the Assigned Proprietary Property."

12. Section 1.1 of the '94 Agreement defines "Proprietary Property" to "mean and include developments, patent rights, copyrights, as well as all patent applications, techniques, methods, processes, apparatus, products, data, trade secrets, confidential information, improvements thereto, modifications thereof, and Know-How, whether

patentable or not, related to the technology described in Exhibit 1 hereto[.]". Exhibit 1 to Section 1.1 of the Agreement states:

> "The technology of "Multivesicular Liposomes having a Biologically Active Substance Encapsulated therein in the Presence of a Hydrochloride," "Heterovesicular Liposomes," "Cyclodextrin Liposomes Encapsulating Pharmacologic Compounds and Methods for their Use," and "Uniform Spherical Multilamellar Liposomes of Defined and Adjustable Size Distribution," including without limitation U.S. patent application Nos. 08/020,483; and 08/078,701; 08/051,135; U.S. Patent No. 5,173,219, respectively, and all divisional, continuation, continuation-in-part, renewal, extension and reissue applications; all foreign counterpart applications and patents; and all U.S. and foreign patents issuing on said applications." DTX-001.0029.

13. As relevant here, Exhibit 1 of the '94 Agreement transferred U.S. Patent Application No. 08/020,483, entitled "Multivesicular Liposomes having a Biologically Active Substance Encapsulated therein in the Presence of a Hydrochloride." The '572 Patent lists the '483 Application under its "Related U.S. Application Data." The '572 Patent further lists "Related U.S. Application Data" that goes back to 1988.

14. The patent and patent applications listed in Exhibit 1 to the '94 Agreement have expired.

15. Section 1.4 of the '94 Agreement defines "Assigned Proprietary Property" to "mean and include the Proprietary Property, including the Patent Rights, Rights in Patents and Know-How, all of which are assigned hereunder to DepoTech."

16. Section 1.6 of the '94 Agreement defines "Assigned Patents" to mean, "both individually and collectively, the United States of America and Foreign Patents included within Proprietary Property and any division, reissue, continuation or extension thereof."

17. Section 3.8 of the '94 Agreement provides:

> "If either DepoTech or RDF files patent applications or otherwise obtains patent rights or copyrights **which relate to** the Assigned Proprietary Property, such patent application, patent rights, or copyrights shall be included in the Assigned Proprietary Property[.]"

18. As consideration for RDF's assignment of the assigned proprietary property, DepoTech agreed to pay RDF a royalty of 2.5% on Gross Revenues during the term of the Agreement.

19. As consideration for RDF's assignment of the assigned proprietary property, DepoTech agreed to pay RDF a royalty of 2.5% on Gross Revenues during the term of the Agreement.

20. Under the '94 Agreement, "Gross Revenues" is defined as "charges actually collected by DepoTech from sales, rental, lease, licensing, maintenance, or production of a Product or from licensing or the use of Assigned Proprietary Property to a third party[.]"

21. Section 1.3 defines "Know-How" as meaning "all information, data, specifications, techniques, software, methods of manufacture, and clinical, as well as diagnostic, information relating to RDF's Proprietary Property which is known to RDF, which RDF is free to disseminate without accounting to others and which is not in the public domain (as defined in Article XIII, paragraphs [a]-[d])."

22. Section 1.7 defines "Product" as "a product or portion of a product that **where made, used[,] or sold embodies an invention there claimed, or which is specifically intended to be used to practice a method or process there claimed in an Assigned Patent** . . . and which is manufactured, and sold by or for" Pacira. (emphasis added).

23. Section 1.8 defines the term "Improvements" as meaning "any improvement and/or modification of the Assigned Proprietary Property that comes within the claims of the Assigned Patents."

24. The '94 Agreement does not mention "DepoFoam."

25. The '94 Agreement also does not reference the Orange Book, Orange Book-listed patents, or any patents relating to the Orange Book.

C. The 1994 Agreement between RDF and Pacira's predecessor, SkyePharma, is amended in 2004.

26. On April 15, 2004, RDF and Skye executed the 2004 Amendment.

27. As relevant here, Section 4.1 of the 2004 Amendment states: "This Agreement (including the Appendices and attachments hereto) together with the Assignment Agreement (including the Appendices and attachments thereto) set out and constitute the entire understanding, warranties and agreement of the parties . . . . In the event of any conflict between the terms of this Agreement and the terms of the Assignment Agreement, the terms hereof shall control." *Id.*

28. Section 1.4 of the 2004 Amendment revised the definition of "Proprietary Property" to read in relevant part as follows:

> "Skye's multivesicular liposome DepoFoam technology which consists of microscopic, spherical particles composed of multiple nonconcentric aqueous chambers encapsulating the biologically active substance therein in the presence or absence of any acid or salt or other compound (the "DepoFoam Technology")," and further stated that "[s]uch DepoFoam Technology shall include (a) the Assigned Proprietary Property or Improvements as defined under the 1994 Agreement, and/or (b) existing and future patent or proprietary rights of Skye in DepoFoam Technology whether or not covered by or subject to the Assignment Agreement." DTX-003.0003.

D. About EXPAREL®: from inception to current day.

29. EXPAREL® is a non-opioid multivesicular liposome (MVL) drug product used to treat acute pain, typically in the surgical setting. The name EXPAREL® is derived from the phrase Extended Pain Relief and provides sustained release of the active ingredient, making it a long-lasting treatment for post-surgical pain. The active ingredient in EXPAREL®, bupivacaine, is a local anesthetic.

30. MVLs are currently the most complex type of liposomes and comprise individual, non-concentric aqueous chambers in a particle. Liposomes are man-made, microscopic, spherical vesicles, composed of amphipathic phospholipids, which have a hydrophilic (water-loving) head and hydrophobic (water-hating) tails.

31. Due to the structural and chemical properties, liposomes are a useful tool in drug delivery because they allow for the sustained release of encapsulated drug products.

32. Liposomes have been known since at least the 1950s and can be classified based on their structural complexity.

33. MVLs consist of a pomegranate-like arrangement of hundreds of chambers, each capable of encapsulating a drug, with that structure enabling delivery of the drug over a sustained period of time as the chambers break.

34. MVLs were first reported in a paper by Sunil Kim, Mitchell S. Turker, Emil Y. Chi, Shifra Sela, and George M. Martin entitled "Preparation of Multivesicular Liposomes" that was published in 1983 in the research journal Biochemica et Biophysica Acta.

35. There are four basic steps to making MVLs: first emulsion, second emulsion, solvent removal, and buffer exchange. Specifically, the steps are as follows:

(i) The first step involves mixing oil (i.e., lipids) and water together to form droplets;

(ii) An external aqueous solution is then added on top of the droplets to force them together to form larger particles that are agglomerations of the droplets. This creates the second emulsion;

(iii) The organic solvent must be removed from the mixture to stabilize the MVLs; and

(iv) Last, the existing buffer must be removed and exchanged with saline.

36. Indeed, these four general steps for the production of MVLs have been known publicly since at least the early 1980s—more than a decade before the '94 Agreement.

37. In 1993, Sunil Kim, Shirin Khatibi, Stephen B. Howell, Cindy McCully, Frank M. Balis, and David G. Poplack published a paper entitled "Prolongation of Drug Exposure in Cerebrospinal Fluid by Encapsulation into DepoFoam" in the research journal Cancer Research. In the 1993 paper, Sunil Kim, et al. used the term "DepoFoam" as another name for multivesicular liposomes, which were described as being "composed of microscopic particles consisting of bilayer lipid membranes enclosing multiple nonconcentric aqueous chambers."

38. MVLs are substantially more difficult to manufacture than conventional liposomes.

39. After an MVL is injected into a wound, the body's physiology degrades the liposome from the outside in and allows for the sustained release of the drug product.

40. The active ingredient in EXPAREL®, bupivacaine, is encapsulated in the MVL chambers, allowing for its gradual release into the surgical site over time as the body degrades the lipid membranes.

41. Pacira began work on creating a commercial-scale process for manufacturing EXPAREL® around 2005. That process was termed the "45L process," based on the volume of the first emulsion.

42. Commercial scale is different from laboratory (or bench) scale.[2] Bench scale is much smaller, sometimes the size of a test tube. There are a "number of innovations and testing and structures, modifications, and many other steps to make a product [at the

[2] The '838 Patent states "commercial scale" and refers to preparation of product in quantities or batches greater than or approximately equal to about a liter (or about 0.1 L for proteinaceous preparations) up to 100 L, for example 1, 10, 25 or 75 L." *See* '838 Patent, PTX-005 at 22. It also defines "laboratory scale," "lab scale," or "bench scale" as "reactions and processes of scales less than about a liter, such as 0.025 L, or 0.2 L." *Id.*

commercial scale]." An MVL or EXPAREL® made at bench scale cannot be injected into a human.

43. EXPAREL® was manufactured utilizing the 45L process at facilities in San Diego, California and Swindon, United Kingdom.

44. EXPAREL® was met with market success since it was launched commercially in 2012, which necessitated the development of larger-scale manufacturing processes.

45. Around 2015, Pacira began exploring alternative methods to manufacturing EXPAREL® in order to meet market demand.

46. From 2017 on, Pacira's development efforts focused on the 200L process.

47. Pacira originally considered building additional 45L process skids to keep up with market demand; there are operational complexities associated with the 45L process, including the fact that Pacira would have needed to run the system twenty-four hours per day, seven days per week, to meet demand. The constant demand on the system means a "lot of labor, a lot of testing, batch record review."

48. Mr. Jeffery Hall explained that the only viable option was to make bigger systems that did not include the same operational constraints as the 45L process.

49. The 4.4-fold increase in capacity in final product volume between the 45L and 200L processes required significant changes to the process.

50. There were difficulties and challenges in Pacira's efforts to scale-up the 45L to the 200L EXPAREL®. Some of those difficulties and challenges included technical challenges such as manufacturing upwards of one hundred development lots prior to submitting the 200L process for FDA approval. The 200L team encountered many failures along the way from the mechanics, to the recipes, to the code. Ultimately, it took Pacira nearly seven years and cost over $100 million to develop the 200L process.

51. To overcome these difficulties, the Pacira team undertook repeated efforts, and trial and error, to upscale EXPAREL®. The team eventually ended up making a desirable product.

52. Because of the 200L process, Pacira will be able to meet the market demand for EXPAREL®.

53. Pacira filed a number of patent applications on the EXPAREL® 200L process and the resulting product. These applications issued as, among others, U.S. Patent Nos.: 11,033,495 (the "'495 Patent"), DTX-027; 11,179,336 (the "'336 Patent"), DTX-029; 11,278,494 (the "'494 Patent"), DTX-030; 11,304,904 (the "'904 Patent"), DTX-031; 11,311,486 (the "'486 Patent"), DTX-032; 11,357,727 (the "'727 Patent"), DTX-033; and 11,185,506 (the "'506 Patent"), PTX-0008 (hereinafter collectively, Pacira's "New Patents").

54. Each of the New Patents are currently listed in the Orange Book for EXPAREL®.

55. To date, Pacira is the only company that is manufacturing multivesicular liposomes at a commercial scale.

E. Pacira brings this declaratory action in 2021.

56. Pacira brought this declaratory action seeking:

> a) That the Court enter a judgment declaring that Pacira does not owe any royalties to RDF with respect to Pacira's EXPAREL® product made after December 24, 2021, under the terms of the Agreements; b) That the Court enter a judgment declaring that Pacira does not owe any royalties to RDF with respect to Pacira's EXPAREL® product made using New Patented Technology, under the terms of the Agreements; c) That the Court enter judgment declaring that any terms of the Agreements that would require Pacira to pay a royalty to RDF with respect to Pacira's EXPAREL® product made after December 24, 2021 or under New Patented Technology are unenforceable; d) That the Court award a refund of any royalties Pacira pays under protest on Pacira's EXPAREL® product made after December 24, 2021, or under New Patented Technology, and order RDF to repay such; e) That the Court award Pacira any and all other relief to which Pacira may show itself to be entitled; and f) That the Court award Pacira any other relief as the Court may deem just, equitable, and proper.

57. In August 2023, I granted Pacira's motion for partial summary judgment after finding that any term of the Agreements between Pacira and RDF requiring Pacira to pay royalties on sales of EXPAREL® made from the 45L process after December 24, 2021 was unenforceable as a violation of public policy. *See* Order, ECF No. 152 at 8–13. In that same Order, I declined to grant RDF's motion for summary judgment as to EXPAREL® utilizing the 200L process. *Id.* at 13–19.

58. Because the parties chose not to define "relate to" in the contract, and the degree of relation under any such definition is unclear from the face of both the '94 Agreement and 2004 Amendment, this case was set for trial to determine if Pacira's New Patents "relate to" the assigned proprietary property set forth in Section 3.8 of the '94 Agreement, and further to determine that if the New Patents are deemed related, whether the '94 Agreement and the 2004 Amendment are nonetheless unenforceable. The question of whether the '495 patent is related to '572 was also an issue to be resolved at trial.

F. The Relevant Patents

1. The '572 patent

59. U.S. Patent No. 5,807,572 (the "'572 Patent") was issued on September 15, 1998, from U.S. Application No. 473,019, filed on June 6, 1995. The '572 Patent states that it is "is a Continuation-in-Part of U.S. Ser. No. . . . 08/020,483, filed Feb. 23, 1993, now abandoned . . . ." The face of the '572 Patent names Sinil Kim and Stephen B. Howell as the inventors.

60. Pacira's predecessor, DepoTech, is listed as the assignee on the cover of the patent.

61. The '572 Patent's claims of priority indicates that it is a "continuation-in-part" of "U.S. Ser. No. 08/020,483," which is listed in Exhibit 1 of the '94 Agreement.

62. The '572 Patent is directed to MVLs that utilize a hydrochloride. The '572 Patent explains that "[t]he prior art also describes methods for producing multivesicular liposomes."

63. The '572 Patent describes a double-emulsion process for making laboratory or bench-scale MVLs, in the presence of a hydrochloride, under non-sterile conditions. That double-emulsion process includes: (1) preparing "a 'water-in-oil' emulsion containing the biologically active substance to be encapsulated" by emulsifying a first aqueous component with a volatile organic solvent containing a lipid component (PTX-0004.0006 at 5:7–9); (2) mixing the water-in-oil emulsion with a second aqueous component "to form solvent spherules suspended in the second aqueous component" (*id.* at 5:19–24); and (3) removing the volatile organic solvent from spherules by "evaporation," "sparging, rotary evaporation, or solvent selective membranes" (*id.* at 5:25–32).

64. The '572 Patent expired on September 15, 2015.

65. The '572 Patent "relate[d] to" the '483 Application because it had a familial relationship with the '483 Application.

2. The '838 Patent

66. U.S. Patent No. 9,585,838 ("'838 Patent"), entitled "Production of Multivesicular Liposomes," issued on March 7, 2017, from U.S. Application No. 11/678,615, filed on February 25, 2007. The face of the '838 Patent names Hartoun Hartounian, Dagmar Meissner, and Clint B. Pepper as the inventors.

67. Pacira is listed as the assignee of the '838 patent.

68. The '838 Patent discloses "[a] new process for preparing MVLs" that is "suitable for manufacturing at commercial scales."

69. The '838 Patent describes the double-emulsion process for making MVLs at laboratory scale. Specifically, it describes "[m]ultivesicular liposomes . . . prepared at commercial scales." The patent defines "commercial scale" as the "preparation of product in quantities or batches greater than or approximately equal to about a liter . . . up to 100 L."

70. Pacira practiced the '838 patent in producing EXPAREL® via the 45L process and the '838 Patent is "incorporated by reference in its entirety" in each of the New Patents.

71. The '838 Patent specifically identifies and claims bupivacaine as a physiologically active substance to be encapsulated.

72. The '838 Patent is not listed in the '94 Agreement and has no familial relationship to the patent and patent applications listed in Exhibit 1 of the '94 Agreement.

73. The '838 Patent expired on December 24, 2021.

74. The '838 Patent is "incorporated by reference in its entirety" in each of the New Patents.

75. Both the '838 Patent and the New Patents disclose the "production of multivesicular [liposomes] encapsulat[ing] drugs at a commercial scale" and the "production of multivesicular liposomes encapsulating bupivacaine [at] a commercial scale."

3. The '495 patent

76. U.S. Patent No. 11,033,495 ("'495 Patent"),[3] entitled "Manufacturing of Bupivacaine Multivesicular Liposomes," issued on June 15, 2021, from U.S. Application No. 17/156,400, filed on January 22, 2021. The face of the '495 Patent names Jeffrey S. Hall, David J. Turnbull, John J. Grigsby, Jr., Soroush M. Ardekani, Paige N. Davis, Louie D.

[3] I only address the '495 and '727 New Patents herein. I reach the same conclusion for all the New Patents, except for the '727 patent, which is addressed separately herein.

Garcia, Stephanie M. Kurz, and Kathleen D.A. Los as the inventors. Pacira is listed as the assignee of the patent.

77. Claim 1 of the '495 Patent is the only independent claim in the '495 Patent, which claims the following:

> 1. **A composition of bupivacaine encapsulated multivesicular liposomes (MVLs) prepared by a commercial scale process**, the commercial scale process comprising:
>
> (a) **mixing a first aqueous solution comprising phosphoric acid with a volatile water-immiscible solvent solution to form a water-in-oil first emulsion**, wherein the volatile water-immiscible solvent solution comprises bupivacaine, 1, 2-dierucoylphosphatidylcholine (DEPC), 1, 2-dipalmitoyl-sn-glycero-3 phospho-rac-(1-glycerol) (DPPG), and at least one neutral lipid;
>
> (b) **mixing the water-in-oil first emulsion with a second aqueous solution to form a water-in-oil-in-water second emulsion**, wherein the second aqueous solution comprises lysine and dextrose;
>
> (c) **removing the volatile water-immiscible solvent from the water in-oil-in-water second emulsion to form a first aqueous suspension of bupivacaine encapsulated MVLs** having a first volume;
>
> (d) **reducing the first volume of the first aqueous suspension of bupivacaine encapsulated MVLs by microfiltration** to provide a second aqueous suspension of bupivacaine encapsulated MVLs having a second volume;
>
> (e) **exchanging the aqueous supernatant of the second aqueous suspension with a saline solution by diafiltration to provide a third aqueous suspension of bupivacaine encapsulated MVLs** having a third volume; and
>
> (f) **further reducing the third volume of the third aqueous suspension by microfiltration to provide a final aqueous suspension of bupivacaine encapsulated MVLs** having a target concentration from about 12.6 mg/mL to about 17.0 mg/mL;

wherein all steps are carried out under aseptic conditions; and

wherein the erucic acid concentration in the composition is about 23 µg/mL or less after the composition is stored at 25° C. for one month.

DTX-027.0020–21 at 22:43–23:12 (emphasis added).

78. The '495 Patent, uses the term "multivesicular liposome" consistent with its plain and ordinary meaning.

4. The '727 Patent

79. The '727 Patent application was filed on January 22, 2021. The '727 Patent (and each of the other New Patents) states that "[e]mbodiments of the present disclosure relate to new and improved commercial scale manufacturing processes for making bupivacaine encapsulated multivesicular liposomes (MVLs)."

80. Specifically, the '727 claims the following:

1. A composition of bupivacaine encapsulated multivesicular liposomes (MVLs) prepared by a process, the process comprising:

(a) **mixing a first aqueous solution comprising phosphoric acid with a volatile water-immiscible solvent solution to form a water-in-oil first emulsion**, wherein the volatile water-immiscible solvent solution comprises bupivacaine, 1, 2-dierucoylphosphatidylcholine (DEPC), 1, 2-dipalmitoyl-sn-glycero-3 phospho-rac-(1-glycerol) (DPPG), and at least one neutral lipid;

(b) **mixing the water-in-oil first emulsion with a second aqueous solution to form a water-in-oil-in-water second emulsion**, wherein the second aqueous solution comprises lysine and dextrose;

(c) **removing the volatile water-immiscible solvent from the water-in-oil-in-water second emulsion to form a first aqueous suspension of bupivacaine encapsulated MVLs** having a first volume;

> (d) **reducing the first volume of the first aqueous suspension of bupivacaine encapsulated MVLs by microfiltration to provide a second aqueous suspension of bupivacaine encapsulated MVLs** having a second volume;
>
> (e) **exchanging the aqueous supernatant of the second aqueous suspension with a saline solution by diafiltration to provide a third aqueous suspension of bupivacaine encapsulated MVLs** having a third volume; and
>
> (f) **further reducing the volume of the third aqueous suspension by microfiltration to provide a final aqueous suspension of bupivacaine encapsulated MVLs** having a target concentration of bupivacaine;
>
> wherein all steps in the process are carried out under aseptic conditions; and
>
> wherein the internal pH of the bupivacaine encapsulated MVLs in the composition is about 5.50.

DTX-033.0020–21 at 22:45–23:12 (emphasis added).

81. Pacira's 45-liter process performs steps (a) through (f) of Claim 1 of the '727 Patent. Steps (a) through (f) "are basic step for making multivesicular liposomes."

82. The '727 Patent also states that "[t]he newly developed processes provide up to 5 folds increase in final product volume as compared to the current process used for the manufacturing of EXPAREL®, which is disclosed in U.S. Pat. No. 9,585,838 and is incorporated by reference in its entirety."

83. The specification for the '727 Patent (and each of the other New Patents) includes FIG. 1A, which discloses "a process flow chart of the formation of an initial aqueous suspension bupivacaine MVLs according to an embodiment of the manufacturing process described herein."

84. The specification for the '727 Patent also includes FIG. 1B, which discloses "a process flow chart of additional steps of concentration, filtration and solvent removal of the initial aqueous suspension of bupivacaine MVLs according to an embodiment of the manufacturing process described herein."

85. The process flow diagrams of FIG. 1A and 1B in the '727 Patent accurately reflect the process flow for the 200L and the 45L process for making EXPAREL® are included below:

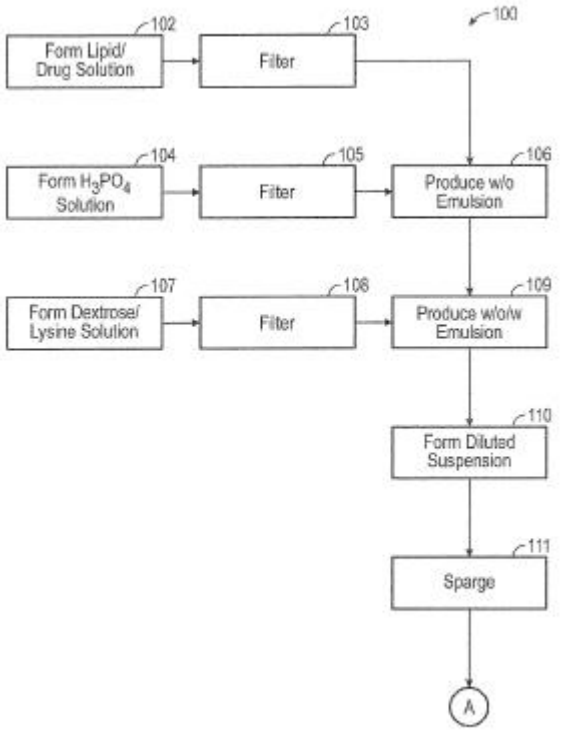

FIG. 1A

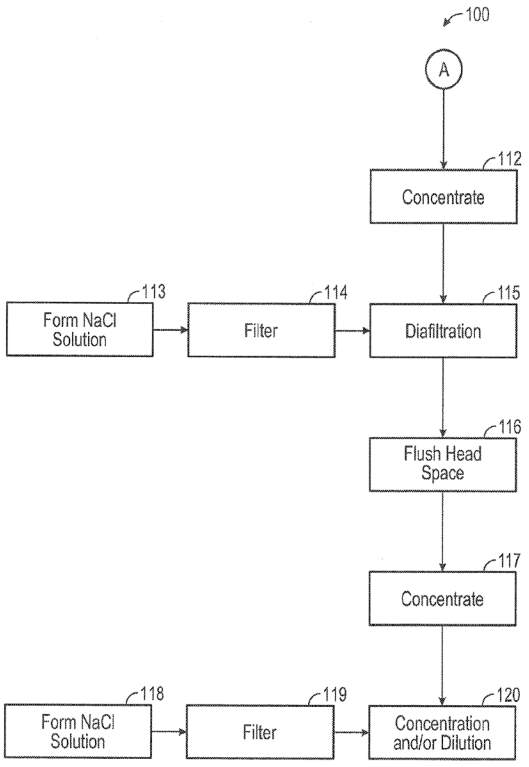

FIG. 1B

G. Summary of relevant witness testimony.[4]

1. Jeffery Hall

86. Pacira called Jeffrey Hall, the named inventor of the New Patents. Mr. Hall currently works at Pacira as the Director of Marketing.

87. Mr. Hall testified about Pacira's significant development work leading to 200L EXPAREL® and the New Patents.

88. Specifically, he testified: (1) that from 2017 onward, Pacira's development efforts focused on the 200L process; (2) that Pacira originally considered building additional 45L process skids to keep up with market demand, but there are operational complexities associated with the 45L process, which would have required Pacira to run the system twenty-four hours per day, seven days per week, to meet demand, meaning a "lot of labor, a lot of testing, batch record review"; and (3) that the only viable option to scale-up production of EXPAREL® was to make bigger systems that did not include the operational constraints of the 45L process.

89. Hall explained that scaling up from 45L EXPAREL® to 200L EXPAREL® was not as easy as scaling up a cookie recipe.

90. Hall also testified that it took Pacira nearly seven years and cost over $100 million to develop the 200L process.

91. I found Hall's testimony to be credible.

2. Dr. Rodney Ho

92. Dr. Rodney Ho testified as an expert witness for Pacira.

93. Dr. Ho earned a Bachelor of Science in Biochemistry from the University of California. He also holds a Master of Science and a Ph.D. in Biochemistry/Drug Delivery and Targeting from the University of Tennessee. While at the University

[4] Other witnesses testified, both at trial and via deposition. Summaries of that testimony is not included here as it did not influence the court's decision.

of Tennessee, Dr. Ho participated in research with members of Oak Ridge National Laboratory. He also completed a Postdoctoral Fellowship in Infectious Diseases at the Stanford University School of Medicine.

94. Dr. Ho is currently employed at the University of Washington, Seattle and at the Fred Hutchinson Cancer Research Center. Dr. Ho's research focuses on making vaccines and other drug combination therapies and is based on lipid-drug interactions. Dr. Ho has been researching lipid-based drugs since 1985.

95. Dr. Ho published his first paper on liposomes in 1987.

96. Dr. Ho testified that a liposome is a general term to describe a spherical particle made of lipids.

97. Dr. Ho's paper on liposomes was foundational for understanding how liposomes, including those used in drug products, can be made stable.

98. Throughout his career, Dr. Ho has published many papers on liposomes and MVLs specifically. Dr. Ho has also personally made MVLs and taught his students how to produce them.

99. The court qualified Dr. Ho as an expert on liposome drug products and their manufacture.

100. Dr. Ho also testified that the '572 Patent is directed to laboratory-scale processes for producing MVLs, and that it would be "very difficult" to commercially manufacture MVLs at the laboratory scale.

101. Dr. Ho then offered three conclusions: (1) Pacira's New Patents describe a new commercial process for making bupivacaine MVLs; (2) Pacira's New Patents describe bupivacaine MVLs having unique characteristics; and (3) Pacira's New Patents are different from the technology of the '572 Patent.

102. Dr. Ho testified that there was a thirty-three-year gap between the first '572 patent and Pacira's New Patents.

103. Dr. Ho testified that making MVLs at the commercial scale required innovations, while acknowledging that there are some similar steps (to include similarities between the 45L and the 200L processes).

104. He also testified that dual and dependent tangential flow filtration, microfiltration by tangential flow filtration, and diafiltration by tangential flow filtration are not discussed in the '572 patent, and noted that bench scale production does not require such processes because "[the manufacturers] spin down to the particles, but it's not sterile. In this process with these filters, you can also get rid of bacteria and many other things in addition to trapping the earlier pre--- so-called preformulation steps where all the things that put in to the manufacturing train is sterile."

105. Dr. Ho also testified about the differences in the solvent removal and sparging at the bench scale versus commercial scale.

106. The court finds that Dr. Ho's testimony was credible.

3. Brian Crozier, Esq.

107. Brian Crozier, Esq., testified on behalf of RDF. Mr. Crozier is an attorney with the law firm of Brorby Crozier & Dobie and is a trustee of the Research Development Foundation.

108. RDF's board of trustees manages the patent and licensing activities of RDF, as well as manages their investments.

109. Mr. Crozier was involved with the formation of RDF, which is a tax-exempt 501(c)(3) nonprofit organization.

110. Mr. Crozier was not personally involved in negotiating the 1994 Agreement between RDF and DepoTech.

111. Although Mr. Crozier reviewed documents relating to the 2004 Amendment, he did not personally participate in telephone calls, conferences, or meetings with SkyePharma regarding the 2004 Amendment.

112. Rather, Mr. Crozier reviewed documents relating to the 2004 Amendment in his role as outside counsel to RDF, over which RDF asserted privilege.

113. The court finds Mr. Crozier's testimony credible.

4. Thomas Brorby, Esq.

114. Thomas Brorby testified as RDF's fact witness via deposition.[5]

115. Mr. Brorby served as a trustee of RDF from 1998 to 2023.

116. Mr. Brorby began working with RDF at its outset in 1988, as someone who incorporated the company.

117. Mr. Brorby also served as outside counsel to RDF and its related organizations. Mr. Brorby worked at the law firm Brorby Crozier & Dobie.

118. Mr. Brorby provided legal services to RDF's related organizations beginning in 1965.

119. I find Mr. Brorby's deposition testimony credible.

5. Dr. Bozena Michniak-Kohn, Ph.D.

120. Dr. Michniak-Kohn testified live at trial as RDF's expert witness.

121. Dr. Michniak-Kohn testified as to the "plain and ordinary meaning" of "multivesicular liposome," which she defined as a "microscopic, spherical lipid vesicle containing multiple, non-concentric aqueous chambers."[6]

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[5] Both RDF and Pacira designated portions of the deposition testimony of Thomas Brorby as part of their respective affirmative trial evidence. To the extent any objections were lodged against Brorby's testimony summarized here, those objections are overruled.

[6] The court notes that it should typically assign claim terms their "'ordinary and customary meaning[,]'" which is "the meaning that the term[s] would have to a person of ordinary skill in the art in question at

122. Dr. Michniak-Kohn also testified regarding the so-called "Amendment Technical Scope" of a twenty-eight-word phrase quoted from the parties' 2004 Amendment, which was provided by counsel for RDF. Dr. Michniak-Kohn described the Amendment Technical Scope as a broad "area of technology" that overlaps with her definition of MVL.

123. Dr. Michniak-Kohn agreed that the only difference between her definition of MVL and her description of the Amendment Technical Scope was that the Amendment Technical Scope includes (1) "a biologically active substance" and (2) the "reinforcing phrase"—"in the presence or absence of any acid, salt, or other compound"—which she admitted does not limit the technical scope in any way.

124. Dr. Michniak-Kohn further admitted that if a substance is "an MVL that encapsulates a biologically active substance," it falls within the Amendment Technical Scope.

125. Dr. Michniak-Kohn opined that the '838 Patent and certain of Pacira's New Patents—namely the '495 Patent, the '336 Patent, the '904 Patent, the '486 Patent, the '496 Patent, and the '727 Patent—each contain a claim covering the technical scope of the 2004 Amendment phrase, as well as a claim that covers MVLs.

126. Dr. Michniak-Kohn testified that the Amendment Technical Scope does not identify or describe any specific invention. She further testified that the Amendment Technical Scope would cover any MVL encapsulating any biologically active substance, regardless of (1) whether the specific MVL technology is novel or already in the public domain—i.e., patentable or not; (2) the particular drug encapsulated, from millions of potential options; (3) any improved or changed characteristics of the MVLs, such as increased stability or internal pH; (4) the composition of the MVLs, which can be affected by the starting materials used in the manufacturing process.

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the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (citations omitted). However, because Dr. Michniak-Kohn testified based on her "plain and ordinary" definition, I reflect her language in my findings. This does not mean that I find that her definition reflects the ordinary and customary meaning of the term "multivesicular liposome."

127. Dr. Michniak-Kohn testified that she did not evaluate whether Pacira' s New Patents disclose an "improved and scaled up process." She also did not evaluate if the disclosed bupivacaine MVLs were more stable than MVLs made by previous processes.

128. Dr. Michniak-Kohn also testified that an MVL product could win the Nobel Prize and still fall within the Amendment Technical Scope.

129. Dr. Michniak-Kohn agreed that a piece of paper merely reciting "microscopic spherical particles composed of multiple non-concentric aqueous chambers encapsulating the biologically active substance therein in the presence or absence of any acid, salt, or other compound" would be covered by the Amendment Technical Scope.

130. Dr. Michniak-Kohn's conclusion that Pacira's New Patents and the '838 Patent are each covered by the Amendment Technical Scope is based solely on the fact that each patent contains a claim falling within a given field of technology—namely MVLs encapsulating a biologically active substance.

131. Finally, Dr. Michniak-Kohn testified that previously, while serving as an expert is previous pharmaceutical litigations, used the term "related to" to mean a patent family member.

132. Dr. Michniak-Kohn testified that that the general process for MVLs was in the public domain as early as 1983.

133. She also testified that she has used the term "related to" to mean a patent family member in other cases where she has testified as a witness.

134. I find Dr. Michniak-Kohn to be credible.

6. Dr. Ashley Stevens

135. Dr. Ashley Stevens testified as RDF's expert witness.

136. Dr. Stevens testified that "related to" is used to describe patent families, however in his opinion, the use of the term "related to" was not a "favored approach" for conveying intellectual property ("IP").

137. During his testimony, Dr. Stevens defined the "IP industry" to include technology transfer professionals, venture capitalists, and IP attorneys.

138. Dr. Stevens also offered opinions regarding assignment agreements.

139. I find Dr. Stevens to be credible.

7. Alessandro Lobbia[7]

140. Mr. Alessandro Lobbia, Pacira's Vice President of Regulatory Affairs-Chemistry, Manufacturing, and Controls, testified as a fact witness via deposition designations in RDF's case-in-chief.

141. Mr. Lobbia testified regarding the similarities between the 45L Process and the 200L Process, stating the two processes "can be used in the same way and meet the same specifications approved in the NDA, and, therefore, can be considered equivalent."[8]

8. David Stack

142. David Stack is Pacira's CEO and Chairman of the Board of Directors. He testified as a fact witness via deposition designation in RDF's case-in-chief.

[7] Pacira objected to this testimony, arguing it was irrelevant as the court already rejected RDF's "field of technology" argument. This objection is overruled as the testimony is relevant to the question of whether the New Patents are related to the assigned proprietary property.

[8] The NDA was not a trial exhibit, therefore the court places no weight on Mr. Lobbia's statement about the NDA.

143. Mr. Stack testified that SkyePharma marketed a drug called DepoCyte, and that it was his understanding that the prefix "Depo" in front of "Cyte" was drawn from DepoTech, the previous manufacturer of DepoCyte.

144. He also testified that Pacira used the name DepoBupivacaine as the generic name for EXPAREL® before it had an approved FDA NDA.

9. Donald Nicholson

145. Mr. Nicholson testified via deposition in RDF's case in chief. Mr. Nicholson was the Chief Financial Officer and finance director for SkyePharma from February 1996 to November of 2006.

146. Mr. Nicholson testified that he believed "DepoFoam" was a word used by Skyepharma for its multivesicular liposome drug delivery technology.[9]

147. Mr. Nicholson also testified that while he worked with Skyepharma, DepoMorphine was still in development, and that that development started before the 2004 Amendment and continued after that agreement was executed.

148. He said the same was true of DepoBupivacaine—that research and development had started on it prior to the 2004 Amendment and continued after it was executed.[10]

10. David Turnbull

149. David Turnbull is a process engineer at Pacira. He testified as a fact witness via deposition designations submitted in RDF's case-in-chief.

150. Mr. Turnbull did not dispute that the '495 patent that the '838 patent disclose the current commercial process as of January 2021 used for manufacturing EXPAREL®.

[9] Pacira's objection to this testimony is overruled. The testimony is relevant to whether the New Patents are related to the assigned proprietary property.

[10] Pacira's objection to this testimony is overruled. The testimony is relevant to whether the New Patents are related to the assigned proprietary property.

151. He further testified that the '495 patent is specific to EXPAREL® at the 200-liter scale and the '838 patent "appear[ed] to be a . . . broader description of the process at a smaller scale."

152. He further confirmed that both the '495 and the '838 patents concern a process for manufacturing "microvesicular" liposomes encapsulating a drug.

II. Conclusions of Law

There is no dispute that MVLs existed for approximately a decade before the parties entered into the '94 and the 2004 Agreements. There is also no dispute that Patents '495 (and the other New Patents), '483, and '572 all follow similar steps for making MVLs. Indeed, it was essentially RDF's position at trial that because all the patents utilize the same steps to make MVLs, the New Patents are related to the assigned proprietary property. In the alternative, RDF argues that because the '838 patent, which no one disputes was utilized to make 45L EXPAREL®, and the New Patents use similar steps, the New Patents are assigned proprietary property. I disagree with both theories.

First, if the basic steps to make MVLs are captured by the '94 Agreement, it seems there would be an obviousness problem[11] with the '572 patent because it would mean that that patent's prior art disclosed the very thing claimed (an MVL), so the claimed invention would have been obvious to a person of ordinary skill in the art as of the relevant date. *See, e.g.*, 35 U.S.C. § 103 (patent may not be obtained if the claimed invention would have been obvious to a person having ordinary skill in the art, based on the prior art, before the effective filing date of the claimed invention). Moreover, the basic steps to making an MVL could not qualify as "know-how" as mentioned in the '94 Agreement because that information was already known at the time the parties entered into the agreement, and therefore would not have been something captured by Pacira's use of those steps in the New Patents. Thus, the basic steps to creating an MVL are neither proprietary property nor assigned proprietary property, so RDF has failed to

[11] The court is not making an obviousness finding here as that is not an issue or question before the court. Rather I mention obviousness to explain RDF's flawed reasoning.

meet its burden showing that the basic steps that result in MVLs alone are sufficient to find that the New Patents are "related to" the assigned proprietary property. As a result, this argument is rejected again.[12]

The court thus turns to the patents themselves. First, there is no dispute the '483 patent is both proprietary property and assigned proprietary property, as it was part of Exhibit 1 to the '94 Agreement. The parties do not dispute that the '572 Patent references the '483 Patent. The court finds that these two patents are related.

The evidence demonstrates, however, that the '572 Patent is different from both the '838 Patent and the New Patents. The following chart is a helpful tool in analyzing why:

	'483 Patent	'572 Patent	'838 Patent	'495 Patent (New Patent)	'727 Patent (New Patent)
Priority Date	Unknown[13]	Priority to 1988	Priority to 1997	Priority to 2021	Priority to 2021
Inventors	Unknown	Kim, Howell	Hartounian, Meissner, Pepper	Hall, Turnball, Grisgby, Ardekani, Davis, Garcia, Kurz, Los	Hall, Turnbull, Grigsby, Ardekani, Davis, Garcia, Kurz, Los
'483 referenced	n/a	Yes	No	No	No
'572 referenced	n/a	n/a	No	No	No
Production Scale	Small (Bench scale)	Small (Bench scale)	Smaller commercial scale (45L process	Larger commercial size (200L process)	Larger commercial size (200L)
Mentions the EXPAREL® Product	No	No	No	Yes	Yes
Specific to Hydrochloride	Yes	Yes	No	No	No
Specific to Bupivacaine	No	No	No	Yes	Yes
Uses Dual Independent Tangential Flow Filtration	Unknown	No	No	Yes	Yes

[12] This is another way to make the same argument about a "field of technology of [MVLs] encapsulating a biologically active substance" that was rejected at summary judgment. *See* ECF No. 152.

[13] A copy of the '483 patent was not provided to the court so certain items are marked as "unknown."

Uses Microfiltration and Diafiltration	Unknown	No	Yes	Yes	Yes
Uses Sterile Nitrogen Sparging	Unknown	No	Yes	Yes	Yes
Uses Aseptic Steps	Unknown	No	Yes	Yes	Yes
Describes MVLs[14] with Elevated Lysine	Unknown	No	No	Yes	Yes
Describes MVLs with Elevated Dextrose	Unknown	No	No	Yes	Yes
Describes MVLs with Elevated pH	Unknown	No	No	Yes	Yes

As demonstrated above, the first two columns, addressing the '483 Patent and the '572 Patent, are shaded in light gray and share some similarities with the middle column, which summarizes some of the '838 Patent characteristics. Both the '483 and the '572 Patents were specific to Hydrochloride (shaded gray), whereas the New Patents are specific to Bupivacaine (not shaded gray). There are also differences between the '572 and the '838 Patents, namely the '572 Patent was specific to Hydrochloride (shaded gray) whereas the '838 Patent was directed to production of MVLs generally (not shaded gray). Thus, what RDF showed is that '838 is fully incorporated into the New Patents, that the end product when utilizing the processes set forth in the '838 Patent and in the New Patents results in EXPAREL®, and that all the patents use similar steps to create MVLs. But as noted above, this does not demonstrate *how* the New Patents are related to the first two patents. Indeed, when looking at the chart from left to right, the commonalities between the '572 Patent and the New Patents disappear. There are *no* shaded boxes showing shared characteristics between the '572 Patent and the New Patents.[15]

[14] The court places less emphasis on this, the elevated lysine, and the elevated dextrose as Pacira's expert witness testified he was given the data from Pacira and did not conduct any testing himself. While given less weight, RDF did not present any witnesses to contradict that the '572 and the '838 did not describe these subjects.

[15] The chart reveals that the New Patents are specific to Bupivacaine and use "Dual Independent Tangential Flow Filtration," whereas '838 and '572 do not. Further, the New Patents use "Microfiltration

Moreover, RDF failed to show that the '838 Patent was assigned proprietary property. First, the evidence shows neither the '838 Patent nor the New Patents share a familial relationship with the '572 Patent. And there was no evidence presented that '838 had any familial relationship to the '483 Patent. Both of RDF's experts testified that "relate to" means familial relationship. Further, although RDF essentially argued that it is clear that the '838 Patent is assigned proprietary property, or perhaps an "improvement" as set forth in Section 1.4 of the 2004 Amendment, the evidence they offered to support that argument is unconvincing. First, RDF only argued that Pacira's royalty payments demonstrate Pacira believed it was covered by the Agreements, but offered no witness to confirm that the royalty payment means the New Patents are *related to* the assigned proprietary property because they incorporate the '838 patent. Pacira's response to this argument, which is not evidence, was that it paid the royalties because the research and development for the 45L process (the '838 Patent) was already underway when it codified the 2004 Amendment. Pacira's position was essentially confirmed by RDF's witness Donald Nicholson, who testified that the research and development for DepoBupivacaine started prior to the 2004 Amendment.[16] Nonetheless, this argument and/or evidence does not demonstrate that the '838 patent, much less the New Patents, is assigned proprietary property, because there was no evidence presented that the '483 and '572 Patents are related to the New Patents. Stated otherwise, RDF did not offer any evidence, beyond the four known steps for making MVLs, to even support that the '838 Patent is assigned proprietary property. And although the '838 Patent is incorporated by reference in the New Patents, and thus RDF proved that the end result product of the '838 Patent and the New Patents was the same drug, RDF failed to overcome the evidence that the '838 patent does not reference the '483 and '572 patents. That alone separates the New Patents from the Agreements' propriety property

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and Diafiltration," "Sterile Nitrogen Sparging," and "Aseptic Steps" as part of the processes, the '572 Patent does not.

[16] I note, too, that even if Pacira *did* interpret the '94 Agreement to include the '838 Patent, Pacira's interpretation of the Agreement is no more binding on the court than RDF's.

and assigned proprietary property. RDF also fails to overcome Pacira's evidence showing the differences in production processes and the significant innovation that went into making the 200L EXPAREL®.

III. Conclusion

The Clerk of Court is kindly instructed to enter judgment in favor of Pacira Pharmaceuticals, Inc. against Research Development Foundation, and to close this case.

Dated: April 16, 2025

Cristina D. Silva
United States District Judge